

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION  
(PCT Rule 61.2)

Date of mailing (day/month/year) 17 April 2001 (17.04.01)	To:  Commissioner US Department of Commerce United States Patent and Trademark Office, PCT 2011 South Clark Place Room CP2/5C24 Arlington, VA 22202 ETATS-UNIS D'AMERIQUE  in its capacity as elected Office
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International application No. PCT/US00/18180	Applicant's or agent's file reference 22001-0003 PCT
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International filing date (day/month/year) 30 June 2000 (30.06.00)	Priority date (day/month/year) 30 June 1999 (30.06.99)
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## Applicant

AN, Jinhua et al

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

23 January 2001 (23.01.01)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Kiwa Mpay
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Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

REC'D 10 SEP 2001

W.P.O.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 22001-0003	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/18180	International filing date (day/month/year) 30/06/2000	Priority date (day/month/year) 30/06/1999	
International Patent Classification (IPC) or national classification and IPC C08B37/00			
Applicant PHARMAGENESIS, INC. et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 23/01/2001	Date of completion of this report 05.09.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Radke, M  Telephone No. +49 89 2399 8677



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/18180

## I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

### Description, pages:

1-35 as originally filed

### Claims, No.:

1-20 as originally filed

### Drawings, sheets:

1/3-3/3 as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description,      pages:
- the claims,      Nos.:

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/18180

the drawings,      sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)): *(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes:	Claims 8,11-15,17-20
	No:	Claims 1-7,9,10,16
Inventive step (IS)	Yes:	Claims 8,20
	No:	Claims 11-15, 17-19
Industrial applicability (IA)	Yes:	Claims 1-9,19,20
	No:	Claims 10-18

### 2. Citations and explanations see separate sheet

## VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:  
see separate sheet

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
see separate sheet

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/18180

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or  
industrial applicability; citations and explanations supporting such statement**

**1. Cited literature**

(a) Reference is made to the following documents:

D1: EP-A-0 441 278

D2: Dissertation Abstracts International (07-01-1987), 47(7), 2891  
& M. McLaughlin, Identification of Immunostimulants derived from the  
Plant Astragalus Membranaceus, dissertation, Texas A&M University,  
1986

D3: US-A-5 589 591

D4: US-A-5 770 217

D5: DATABASE CHEMICAL ABSTRACTS, AN 115:105995 & CN-A-1 047 296

D6: US-A-4 944 946

(b) In the following arguments, page or column A, lines B to C will be cited as A/B-C.

**2. Novelty**

(a) Document D1 mentions at 1/41-46: "In previous studies (Dissertation Thesis, McLaughlin, 1986), it had been possible to isolate from the roots of **Astragalus membranaceus** some polysaccharides characterized by **molecular weights of about 25000 daltons** which consisted of **galactose, arabinose and xylose** and were endowed with generic immunomodulating properties." (Emphasis added; see also the respective dissertation abstract D2).

It is not probable that a different polysaccharide is isolated only due to a certain place where the plant is grown (see present claim 3) or due to a certain age of the plant (see present claim 4).

Due to this disclosure, the subject-matter of **claims 1 to 6** is not novel.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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(b) Document D3 discloses endotoxin-free arabinogalactan (from *Larix occidentalis*) which is made by cutting off the fractions having molecular weights lower than 10 kDa and higher than 100 kDa by ultrafiltration (see D3, examples 1 and 2 and claims 1 to 8).

There is no indication in the present application that the arabinogalactan obtained from *Larix occidentalis* is different from that isolated from *Astragalus membranaceus*.

D3 mentions that the arabinogalactan thus purified is useful for intravenous injection in therapy (see D3, 2/10-11, 3/21-24 and 1/31-49), e.g. in combination with an antiviral agent (see D3, 1/42-47).

For this reason, the subject-matter of **claims 1, 7, 9, 10 and 16** is not deemed to be novel in view of D3.

### **3. Inventive step**

(a) D4 discloses at 5/23-45 that *Astragalus membranaceus* contains at least 8 major polysaccharide fractions which stimulate interferon production, mononuclear cell (both the granulocytic and lymphocytic series) proliferation, restore the immune system after chemotherapy and prevent hepatotoxicity after radiation and chemotherapy.

It was thus obvious to the expert to use the arabinogalactans disclosed in D1 for the purpose disclosed in D4.

Consequently, the subject-matter of **claims 11 to 15** is not based on an inventive step.

(b) Document D5 recommends the use of an immunostimulant containing

- (1) Interleukin-2 (IL-2) and
- (2) substance F3 extracted from *Astragalus membranaceus* for treating cancer and AIDS.

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As is apparent from D1, 1/24-39, substance F3 contains carbohydrates having molecular weights of from 20 to 25 kDa. This carbohydrate most likely contains the arabinogalactan of the molecular weight of about 25 kDa mentioned in D1, 1/41-48.

It was thus most obvious to the expert to administer said arabinogalactan disclosed in D1 (and D2) in combination with an interleukin as disclosed in D5.

For this reason, the subject-matter of **claims 17 and 18** is not based on an inventive step.

- (c) The method of **claim 19** comprises standard isolation and purification steps disclosed in D6, example 1 and D3, 3/1-2. The subject-matter of this claim is thus not deemed to be inventive.
- (d) The prior art does, however, not disclose an arabinogalactan protein composition (AGPC) obtained from a purified arabinogalactan and having a molecular weight of at least 100 kDa. The applicant has shown that AGPC promotes red blood cell and platelet recovery in irradiated mice (see 23/3-9 of the present application).

As a consequence of this, the subject-matter of **claims 8 and 20** is based on an inventive step.

**4. Industrial applicability**

For the assessment of the present **claims 10 to 18** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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**Re Item VII**

**Certain defects in the international application**

1. The patent number cited at 2/18 is obviously wrong. It should be amended to read 5,268,467.
2. The expression "The disclosure of these and other documents ... are incorporated herein by reference" at 3/23-24 leaves doubt as to the actual disclosure of the present application. Said expression should be deleted.

**Re Item VIII**

**Certain observations on the international application**

The statement in the description at 35/13-17 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/18180

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C08B37/00 A61K31/715

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C08B A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DISSERTATION ABSTRACTS INTERNATIONAL, vol. 47, no. 7, 7 January 1987 (1987-01-07), page 2891 XP000942629 & MCLAUGHLIN, MICHAEL ATKINS: "Identification of Immunostimulants derived from Astragalus Membranaceus" 1986 , DISSERTATION, TEXAS A & M UNIVERSITY , COLLEGE STATION, TX, US ----	1-20
X	EP 0 441 278 A (INDENA SPA) 14 August 1991 (1991-08-14) column 1, line 24-48 ----	1-6
Y	----	11-15, 17-19 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

24 October 2000

08/11/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Radke, M

## INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 589 591 A (LEWIS JEROME M) 31 December 1996 (1996-12-31) cited in the application column 2, line 10,11; example 1 column 1, line 41-45 ---	1,7,9, 10,16
Y	US 5 770 217 A (KUTILEK III FRANK J ET AL) 23 June 1998 (1998-06-23) column 5, line 23-45 ---	11-15
Y	DATABASE CHEMICAL ABSTRACTS 'Online! Chemical Abstracts Service, Columbus OH/US; AN 115:105995, XP002150924 abstract & CN 1 047 296 A (THE PEOPLES REPUBLIC OF CHINA) 28 November 1990 (1990-11-28) ---	17,18
Y	US 4 944 946 A (LIU YAGUANG) 31 July 1990 (1990-07-31) example 1 ---	19
A	EP 0 511 932 A (ANDROMACO LAB) 4 November 1992 (1992-11-04) page 2, line 45,46; claim 5 ---	9-18
A	US 5 116 969 A (ADAMS MARK F ET AL) 26 May 1992 (1992-05-26) cited in the application example 2 -----	1,5

# INTERNATIONAL SEARCH REPORT

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0441278	A	14-08-1991	IT 1238685 B CA 2035948 A JP 5039305 A	01-09-1993 10-08-1991 19-02-1993
US 5589591	A	31-12-1996	US 5554386 A US 5336506 A US 5478576 A US 5141739 A US 4827945 A US 4770183 A AU 2700195 A CN 1150761 A WO 9534325 A ZA 9504925 A US 5490991 A AT 151991 T CA 2097589 A,C DE 69125848 D DE 69125848 T DE 563249 T DK 563249 T EP 0563249 A ES 2059299 T GR 94300001 T GR 3023358 T JP 6503347 T WO 9211037 A CA 2105068 A DE 578765 T EP 0578765 A ES 2061423 T GR 94300022 T JP 6506230 T WO 9217216 A AT 139431 T DE 68926708 D DE 68926708 T EP 0381742 A EP 0670167 A JP 4501218 T WO 9001295 A US 5679323 A US 5262176 A US 5284646 A US 5352432 A US 5342607 A AT 143604 T CA 1301063 A DE 3751918 D DE 3751918 T EP 0275285 A JP 1500196 T NO 880931 A WO 8800060 A	10-09-1996 09-08-1994 26-12-1995 25-08-1992 09-05-1989 13-09-1988 05-01-1996 28-05-1997 21-12-1995 13-02-1996 15-05-1997 20-06-1992 28-05-1997 31-07-1997 03-03-1994 03-11-1997 06-10-1993 16-11-1994 28-02-1994 29-08-1997 14-04-1994 09-07-1992 03-10-1992 26-05-1994 19-01-1994 16-12-1994 29-04-1994 14-07-1994 15-10-1992 15-07-1996 25-07-1996 31-10-1996 16-08-1990 06-09-1995 05-03-1992 22-02-1990 21-10-1997 16-11-1993 08-02-1994 04-10-1994 30-08-1994 15-10-1996 19-05-1992 07-11-1996 20-03-1997 27-07-1988 26-01-1989 02-03-1988 14-01-1988
US 5770217	A	23-06-1998	NONE	
CN 1047296	A	28-11-1990	NONE	

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/18180

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 4944946 A	31-07-1990	US	4886666 A	12-12-1989
		US	4944945 A	31-07-1990
		US	4985247 A	15-01-1991
EP 0511932 A	04-11-1992	ES	2049561 A	16-04-1994
		JP	5178751 A	20-07-1993
		NO	921583 A	28-10-1992
US 5116969 A	26-05-1992	NONE		